fMRI is 7

What have we learned?

What don't we know?

What might we find out?

Peter A. Bandettini

fMRI is 7

Brief History….

Blood T2 sensitive to oxygenation.

-T1 not changed.

-therefore bulk susc. effect (not dipolar interaction)

Thulborn, K. R., J. C. Waterton, et al. (1982). “Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field.” Biochim. Biophys. Acta. **714**: 265-270.

"BOLD contrast" coined.

Ogawa, S., T. M. Lee, et al. (1990). “Brain magnetic resonance imaging with contrast dependent on blood oxygenation.” Proc. Natl. Acad. Sci. USA **87**: 9868-9872.

Early work in rats and cats.

Ogawa, S. and T.-M. Lee (1990). “Magnetic resonance imaging of blood vessels at high fields: in vivo and in vitro measurements and image simulation.” Magn. Reson. Med **16**: 9-18.

Ogawa predicted brain mapping in humans...

(predicted negative signal change with activation though)

Turner, R., D. LeBihan, et al. (1991). “Echo-planar time course MRI of cat brain oxygenation changes.” Magn. Reson. Med. **22**: 159-166.

First Results in mapping activation in humans:

1. MGH using Gadolinium contrast: 1990-91.

2. MGH using BOLD: May 21, 1991

3. Minnesota using BOLD: ??

4. MCW using BOLD: Sept 9, 1991

First Presentations:

August, 1991 SMRM San Francisco (Tom Brady, Robert Weisskoff)

Tom Brady: "...and we don't know what causes it.."

First Papers: June, 1992.

Kwong, K. K., J. W. Belliveau, et al. (1992). "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation." Proc. Natl. Acad. Sci. USA. **89**: 5675-5679.

Ogawa, S., D. W. Tank, et al. (1992). "Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging." Proc. Natl. Acad. Sci. USA. **89**: 5951-5955.

Bandettini, P. A., E. C. Wong, R. S. Hinks, R. S. Tikosfky, J. S. Hyde. (1992). "Time course EPI of human brain function during task activation." Magn. Reson. Med. **25**: 390-397.

What have we learned?

1. About human physiology?

-confirmed basic results in PET (Fox et al), and optical Imaging (Frostig et al):

blood oxygenation increases (OEF decreases) during activation…

-BOLD and flow response fast, consistent, and sustained.

-BOLD and flow are roughly proportional to integrated neuronal activity (when modulated in a single region).

-more questions opened up….

why increased oxygenation?
why post undershoot?
why pre-undershoot?
baseline oscillations?

About fMRI contrast?

-BOLD magnitude is proportional to:

blood volume, resolution hct, pO2, field strength, pulse sequence,TE, diffusion weighting, coupling mechanisms?

-Types of flow contrast:

perfusion contrast
inflow contrast

-Spatial Resolution:

"downstream" vein effects
BOLD and flow don't completely overlap.
Overlap is assumed to be capillaries.

-Dynamics:

"impulse response" derived, but...
nonlinearities exist (stim duration < 4 sec)
variability is <100 ms within each voxel
variability is > 4 sec across voxels
post - undershoot appears consistantly
pre - undershoot still elusive

-Physiologic stress:

CO2, apnea, etc..gives predictable response
used with flow and BOLD, can give CMRO2

-Noise:

contains information....

About fMRI methods?

-Pulse sequence:

optimal contrast,
GE w/ TE ≈ T2, TR ≈ 1 to 3 sec.*

Artifact sources:

shim, reconstruction, eddy currents
clock synchronization

Temporal stability:

respiratory, cardiac, low freq. fluctuations
motion, scanner stability,
pulse sequence type:
(i.e. spin-echo, spiral scan, single shot)

Image acquisition limits:

volume coverage
temporal sampling rate

Functional contrast:

spin-echo, gradient-echo, assymetric-spin echo, many more.....

Optimal field strength:

trade-offs: shim, volume coverage, sensitivity, signal to noise, resolution

Post Processing:

Motion correction methods
Statistics (noise and signal are not that simple)
Correlation analysis
Multiplexing tasks (freq. encoding)
"Phase encoding" of tasks
Multiple orthogonal tasks
"Event related" fMRI
Stimulus Input Deconvolution
Real time fMRI

What don't we know?

About human physiology?

Neuronal - hemodynamic coupling:

-why does blood flow increase?
-how consistant is it over space?
-how consistant is it across task modulation?
-is it dependent on observed spatial scale?

-relationship between number and rate of firing neurons and BOLD and/or flow response.
(spatial/temporal scale?)

About fMRI contrast?

Retails of:

field strength dependence
TE dependence
upper temporal and spatial resolution
spin-echo vs. gradient-echo
diffusion weighting effects
dep of functional contrast (ΔS/noise) across res.
noise

Reasons for:

post-undershoot
pre-undershoot
negative signal changes

-how to robustly measure and control for
relevant variables in BOLD
(i.e. how to calibrate the fMRI response)

Physiologic stress:
what more physiologic information can we derive from a map created by CO2, apnea, etc.

About fMRI methods?

-Pulse sequence:

Optimal tradeoff between physiologic information, sensitivity, brain coverage, and overall image quality

-Processing:

For randomized event - related input, what is the optimal time series type?

-Scanners:

Best field strength? (tradeoff between sensitivity, image quality, stability, and brain coverage)

Lots of room to improve shim.

About how the brain is organized?

Maps of location, relative dynamics, relative sensitivity to modulated input, and habitutation.

but…

Limited to a relativly coarse and slow spatial and temporal scale. Can we really derive principles (and not just descriptions) of how the brain is organized from these??

Also:

Clinical Applications?

Compliment or a better indicator than behavioral measures of mental disorders?

Drug effects?

About how the brain is organized?

Maps of location (coarse resolution), relative dynamics (slow time scale), and relative sensitivity to modulated input over time.

Higher resolution and better sensitivity than PET

Also, repeated trials in same subject has allowed new realm of studies.

Clinical Applications.

presurgical mapping
replacing wada test

What might we find out?

Meth. to characterize hemodyamic variables (hct, volume, etc…) on a voxel wise basis.

Upper temporal and spatial res.
-and methods for extraction

Quantitative hemodyamics:

- **inflow**
- **flow**
- **blood volume**
- **oxygenation**

Quantitative metabolism:

- **resting and changes in CMRO2**

Optimal field strength.

Set of standard pulse sequences

Pre, Post undershoot

Neuronal input strategies optimized to post processing methods.

Noise characteristics and uses.

Meth. to detect neuronal currents.

Correlation of task, rest, and physiologic stress responses to specific clinical cases.

fMRI will help to answer coupling questions.

much improved shimming

real time

Extensive clinical use of baseline flow, volume, metabolism, hemodynamic reactivity (CO_2 effects..) information.

Increased clinical use of brain activation data. (absolute necessity for real time fMRI)

Research Directions:

1. Calibration and quantitation of fMRI signal magnitude and latency.

-matrix of registered, voxel-wise hemodynamic/metabolic/neuronal information in a single session

-sophisticated models of coupling, hemodynamic, MRI signal models.

2. Crafting of:

Pulse-sequence, Neuronal input, subject physiology, subject response,and post processing methods.

3. Correlation of MRI derived baseline and activation-induced information with disorders and therapy.

4. Shimming, temporal stability, RF coil arrays, noise reduction, embedded multiple contrast, pulse sequence tailored gradient coils.